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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,852	07/15/2003	Mark Chee	67234-015	2545

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 07/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,852	CHEE ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-103* is/are pending in the application.

4a) Of the above claim(s) *1-34 and 53-103* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 4/28/2006 to the Office action has been entered. Claims 1-103 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 35-52 in the reply filed on 4/28/06 is acknowledged.

2. Claims 1-34, and 53-103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/28/06.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 35-52 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5, 6, 11, and 13-30 of copending Application

No. 10194958. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of detecting the relative amount of two or more target sequences in which the method comprises hybridizing a first and second pair of probes with first and second target sequence in an initial population to form first and second ligation complexes, ligating the first and the second ligation complexes to form first and second ligated probes, linearly amplifying the first and second ligated probes to produce first and second amplicon and determining a relative amount of the first and second amplicons, while claims 5, 6, 11, and 13-30 of copending Application No. 10/194,958 are drawn to a method which comprises similar method steps with the instant claims. The differences between two inventions are that claims 5, 6, 11, and 13-30 of copending Application No. 10/194,958 specify a plurality of target nucleic acid sequences each comprising from 3' to 5' a first, second and third target domain, the sets of probes for each target sequence in which a first probe comprising from 5'to 3', a first domain comprising a first universal priming sequence and a second domain comprising a sequence complementary to the first target domain and a sequence complementary to the second target domain and a second probe comprising a first domain complementary to the third target domain to form a set of first hybridization complexes and under conditions a second hybridization complexes is formed by the hybridization of the first probe to the second target domain of the target sequence and then ligate the extended first probes to the second probes to form amplification templates which is amplified to form amplicons and the amplicons are detected. Therefore, the instant claims 35-52 and claims 5, 6, 11, and 13-30 of copending Application No. 10/194,958 are related as genus-species.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 35, 39, 41, 42, 43, 44, 47, and 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 10, 18, 20-22, 23-24, 32, 39-40, 42-46, 54, and 64-66 of copending Application No. 10864935. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of detecting the relative amount of two or more target sequences in which the method comprises hybridizing a first and a second pair of probes with first and second target sequence in an initial population to form first and second ligation complexes, ligating the first and the second ligation complexes to form first and second ligated probes, linearly amplifying the first and second ligated probes to produce first and second amplicon and determining a relative amount of the first and second amplicons. The first and the second pair of ligation probes of the instant invention each comprises a first target-specific sequences of a first probe, a second target-specific sequence of a second probe, a universal priming site and an adaptor sequence. Claims 1-2, 10, 18, 20-22, 23-24, 32, 39-40, 42-46, 54, and 64-66 of copending Application No. 10864935 are drawn a method of determining the identification of a nucleotide at a detection position in a target sequence. Both inventions have similar method steps. The differences between two inventions are the method of claims 1-2, 10, 18, 20-22, 23-24, 32, 39-40, 42-46, 54, and 64-66 of copending Application No. 10864935 apply a probe set to form a hybridization complex, the probe set comprising a first probe having a first portion containing an upstream universal priming site (UUP), a second portion containing a first target specific sequence and a detection position and second probe having a first portion

containing a downstream universal priming site and a second portion containing a second target specific sequence, the probe set comprises at least one adapter sequence. The limitations of probes used in the instant invention are inherent that the probes have these specific limitations as recited in claim 1 of copending Application No. 10864935. Thus the instant inventions and claims 1-2, 10, 18, 20-22, 23-24, 32, 39-40, 42-46, 54, and 64-66 of copending Application No. 10864935 are related as genus-species.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 35-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 48 is vague and indefinite because of the phrase "said plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536". It is unclear what is meant by these numbers.

b. Claims 35-52 are vague and indefinite because it is unclear whether or not the first and second amplicons are quantified separately. Clarification is required.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 35-42, 45-46, and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar et al. (5,593,840, issued January 14, 1997) in view of Phillip et al. (6,017,738, issued January 25, 2000).

Bhatnagar et al. disclose a process for amplifying nucleic acid sequence from a DNA or RNA template. The process allows to efficiently detect a particular point mutation (See the abstract). The process provides primers comprising a first primer which is substantially complementary to first segment at a first end of the target nucleic acid sequence and a second primer, which is substantially complementary to a second segment at a second end of the target nucleic acid sequence. The first and second primers are hybridized to the target nucleic acid sequence (See column 3, lines 11-30). The second primer (oligo 2) is extended and then ligated to the first primer (See fig. 3) to produce fused amplification products (See column 3, lines 31-34). The fused amplification products are amplified (See column 3, lines 35-44). The process

also provides four different nucleotide bases (See column 3, lines 27). The amplified fused amplification products are detected by detectable signal (See column7, lines 8-22). The primers may be labeled using a marker (See column 9, lines 17-23, column 15, lines 17-54). The amplified stands may be labeled with different markers (See column 9, lines 24-29). The extension of a primer by polymerase can be blocked (See column 7, lines 32-39).

Bhatnagar et al. do not explicitly disclose linear amplification of the first and second ligated probe to produce first and second amplicons. However, in the disclosure of Bhatanagar et al. the fused amplification product from the target nucleic acid sequence is extended by a third primer (See column 3, lines 36-44). This teaching is inherent that there is a single primer amplification, which is linear amplification.

Bhatnagar et al. also do not explicitly disclose a universal priming site in a probe. Based on the definition in the specification, the universal priming site means a sequence of the probe, which will bind to a primer for amplification (See 20040121364, [0084]). Thus the features of the primers of Bhatanagar et al. satisfy the limitations of the probe of the instant invention.

Bhatnagar et al. also do not explicitly disclose a second universal priming site in the first probe or second probe. Based upon the discussion above and there is no physical features for the second universal priming site, the first and the second probe are interpreted that the first or second probe has a second universal priming site.

Bhatnagar et al. do not explicitly disclose the probe having an adapter sequence. There is no physical features for the adapter sequence in the specification and there is only function description for the adapter sequence, for example, for hybridization (See 20040121364, [0072]). Thus the features of the primers of Bhatanagar et al. satisfy the limitations of the probe.

Bhatnagar et al. do not disclose determining a relative amount of the first and second amplicons and the universal priming site comprising a RNA polymerase priming site corresponding to T7, T4 T3, and SP6 RNA polymerase.

Phillip et al. disclose a method for detecting a target nucleic acid sequence in which a first primer hybridizing to the target nucleic acid sequence is immobilized and a second primer is provided to hybridize the target nucleic acid sequence in the opposite direction and the second primer is labeled (See the Abstract). The incorporated label in the amplified nucleic acid sequence allows detection and quantification of the amplified nucleic acid (See column 2, lines 1-15). The nucleic acid amplification methods applied to the solid phase amplification process (See column 6, lines 41-58) include NASBA. NASBA amplification method has a transcription step in vitro (See fig. 3). The primer used in NASBA has a RNA promoter sequence corresponding to T7 RNA polymerase (See column 7, lines 12-18). This teaching reads on the limitation recited in claims 36 and 37 in which universal priming site comprises a RNA polymerase priming site corresponding to T7, T4, T3, SP6 RNA polymerase.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of Bhatnagar et al. to determine the amount of the first amplicon and the second amplicon because as disclosed by the teachings of Philip et al. the incorporated label in the amplified nucleic acid sequence allows detection and quantification of the amplified nucleic acid (See column 2, lines 1-15). It would have been prima facie obvious to determine the relative amount of the first and the second amplicons for detecting the relative amount of two or more target sequences.

10. Claims 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar et al. (5,593,840, issued January 14, 1997) in view of Phillip et al. (6,017,738, issued January 25, 2000) as applied to claims 35-42, 45-46, and 49-52 above, and further in view of Barany et al. (6,027,889, issued February 2000).

The teachings of Bhatnagar et al. and Phillip et al. are set forth in section 9 above. Bhatnagar et al. do not disclose the target nucleic acid sequences comprise a solid support, immobilizing the amplification templates or amplicons to a solid support with a capture probe.

Barany et al. disclose the detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reaction (See the Abstract). The invention provides a primary PCR/secondary PCR/LDR process in which the amplified products are immobilized to an addressable array (See column 13, lines 23-26) by the capture oligonucleotide probes which is complementary to a nucleotide sequence across the ligation junction (See column 24, lines 55-60). The extended products are captured on an array of capture oligonucleotide addresses (See column 24, line 55-58). It suggests that the target nucleic acid, which is extended products, comprises a solid support as recited in claims 43-44.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the addressable array of Barany et al. to the method of Bhatnagar et al. for determining the relative amount of the first and the second amplicons. Barany et al. states that by using the addressable array, the presence of one or more target nucleotide sequences in a sample is detected (See column 27, lines 15-19). It would have been prima facie obvious to apply the array of Barany et al. to the method of Bhatnagar et al. for determining the relative amount of the first and the second amplicons.

11. Claims 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar et al. (5,593,840, issued January 14, 1997) in view of Phillip et al. (6,017,738, issued January 25, 2000) as applied to claims 35-42, 45-46, and 49-52, and further in view of Akhavan-Tafti (5,998,175, issued December 7, 1999).

The teachings of Bhatnagar et al. and Philip et al. are set forth in section 9 above. Bhatnagar et al. and Philip et al. do not disclose a plurality of pairs of ligation probes with a plurality of target sequences to form a plurality of ligation complexes, each of the plurality comprises more than two and the plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536.

Akhavan-Taffti discloses a method of synthesizing polynucleotides involving the simultaneous ligation of a set of oligomer 5'-phosphates onto a template-bound primer. The ligation is performed with a ligase enzyme (See the abstract). This teaching is inherent that a plurality of pairs of ligation probes with a plurality of target sequences is to form a plurality of ligation complexes and each of the plurality comprises more than two (See fig. 2). The disclosure of Akhavan-Taffti also discussed the library can contain all 4^n possible oligomers (See column 5, lines 55-59 and column 6, lines 22-43).

One of ordinary skill in the art would have been motivated to apply a plurality of pair of ligation probes with a plurality of target sequences to form a plurality of ligation complexes in which the plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536 as taught by Akhavan-Taffti because the amplification method of Akhavan-Taffti can be use to copy DNA or RNA linearly or exponentially (See column 1, lines 15-17). It would have been prima facie obvious to apply a plurality of pair of ligation probes with a plurality of target sequences to form

a plurality of ligation complexes in which the plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536.

Summary

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung J.T
July 9, 2006

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
7/13/06